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Case Report

Yolk-sac carcinoma mimicking sacrococcygeal teratoma in an infant ☆,☆☆

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ABSTRACT

Extragonadal germ cell tumors (GCTs) are rare, accounting for 1% to 5% of all GCTs, with malignant sacrococcygeal yolk sac tumors (SCYSTs) being part of this uncommon subset. These tumors primarily occur in children and young adults and are known for their aggressive behavior, necessitating early diagnosis and prompt treatment. In this case report, we present the case of an 8-month-old female who presented with mild abdominal distension and a 3-week history of difficulty passing urine. Imaging revealed a pelvic mass originating from the coccyx, compressing the urinary bladder. The mass was surgically excised, and histopathological analysis confirmed a malignant yolk sac tumor with positive margins. The patient received adjuvant chemotherapy postsurgery. Despite treatment, follow-up scans showed residual tumor tissue, leading to a second tumor resection. Surveillance was continued using Alpha Fetoprotein (AFP) levels as a marker, which revealed a relapse of the tumor. Subsequent imaging confirmed a growing tumor, and the patient was scheduled for second-line chemotherapy. Management of SCYSTs is complex and requires a multidisciplinary approach, including surgeons, oncologists, radiologists, and pathologists. While relapse is rare, it poses a significant challenge for treatment, underscoring the need for clear and updated guidelines for managing relapsed cases.

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Introduction

Malignant yolk-sac tumors (MYSTs), also referred to as endodermal sinus tumors, are rare, aggressive germ cell tumors that predominantly affect children and young adults. First described by Teilum in 1959, these tumors are noted for their histological resemblance to the yolk sac of the developing embryo [1]. Typically, MYSTs originate in the gonads, with the testes being the most common site in males and the ovaries in females [2]. However, extragonadal occurrences, though rare, have been reported in locations such as the mediastinum, sacrococcygeal region, and retroperitoneum [3,4]. Extragonadal germ-cell tumors (GCTs) represent only 1% to 5% of all GCTs, making them relatively uncommon [5].

Malignant yolk sac tumors (MYSTs) present significant diagnostic and therapeutic challenges due to their diverse clinical manifestations and aggressive growth. Early diagnosis is crucial for effective management and improving patient outcomes. Despite their rarity, MYSTs are important to recognize because of their rapid progression, which can lead to poor prognosis if not promptly treated [3].

In this case report, we present a malignant yolk sac tumor arising in the sacrococcygeal region of an 8-month-old female. We explore the clinical presentation, diagnostic approach, management strategies, and outcomes of this case, emphasizing the need for early detection and multidisciplinary collaboration in managing such aggressive tumors. Through this report, we hope to contribute to the expanding knowledge of MYSTs and highlight the complexities involved in treating these rare neoplasms.

This manuscript was prepared following the CARE guidelines (https://www.care-statement.org).

Case presentation

An 8-month-old female was referred to our tertiary center from a primary health facility with a 3-week history of progressively worsening abdominal distension and an inability to pass urine. Initial urethral catheterization was performed, resulting in the drainage of clear urine and the resolution of the abdominal distension. However, upon catheter removal, urinary retention recurred, necessitating the re-insertion of the catheter. The patient had no history of vomiting and maintained normal bowel habits. There was a notable history of poor weight gain since birth, along with delayed developmental milestones, specifically delayed sitting up and crawling. An abdominal-pelvic ultrasound revealed the presence of a pelvic mass, prompting her referral to our center for further evaluation and management.

On arrival, the patient was alert and active but cachexic. She appeared well-hydrated, afebrile, and had no signs of pallor, jaundice, or dyspnea. Scoliosis was noted. Her abdomen was slightly distended, moving with respiration, soft, nontender, with no palpable organomegaly. The external genitalia were normal for a female, and a urethral catheter was in place, draining clear, amber-colored urine. There were no palpable peripheral lymph nodes.

The anal verge anatomy was displaced slightly anteriorly due to a perineal bulge, which was hard and painless on palpation. The anal sphincter was loose, and the rectal mucosa felt free, with the gloved finger stained with fecal matter. Neurologically, the patient exhibited weakness in both lower limbs, along with instability of the right ankle joint.

Her laboratory investigations revealed a hemoglobin level of 10.6 g/dL (reference range: 12.1-15.1 g/dL), a normal leukocyte count of 8.74 $\times$ 10^9/L, and a reduced platelet count of 110 $\times$ 10^9/L (reference range: 150-450 $\times$ 109/L). Serum urea and creatinine levels were within normal ranges. Serum sodium was mildly low at 128.9 mmol/L (reference range: 135-145 mmol/L), while serum potassium was within normal limits at 4.05 mmol/L (reference range: 3.5-5.5 mmol/L). Liver enzymes showed an elevated aspartate transaminase (AST) of 44.6 U/L (reference range: 8-33 U/L), and alanine aminotransferase (ALT) was normal at 19.0 U/L (reference range: 4-36 U/L).

A CT scan of the chest, abdomen, and pelvis revealed a large heterogeneous, enhancing mass within the pelvis, originating from the sacrococcygeal region. The mass was displacing the urinary bladder, rectum, and large bowel anteriorly, measuring 7.6 $\times$ 5.3 $\times$ 8.4 cm, and extending bilaterally into the greater sciatic foramina (Fig. 1).

This clinical presentation and findings were suggestive of a type IV sacrococcygeal teratoma, infantile scoliosis and chronic malnutrition. Pediatricians were consulted for management of malnutrition and was started on plumpy nuts. She was then scheduled for elective wide local excision (WLE). Intraoperatively, in prone position, an inverted V shaped incision was made over the lower back. Subcutaneous tissue was bluntly dissected away from the tumor capsule. A type IV tumor was found, extending into the pelvis on either side as well as involving the coccyx. It was highly vascularized. The tumor was dissected away along with its capsule and the coccyx; small remnants were left deep in the pelvis. Cavity was washed with warm saline and a drain was placed. Incision was closed in layers. Excised tumor was sent for histopathology.

Postoperatively patient was kept on intravenous antibiotics for 3 days and analgesia as per local protocol. After 3 days daily wound dressing with application of mupirocin cream was done, the wound healed uneventfully (Fig. 2). Histopathological examination displayed malignant primitive germ cell tumor composed of loose mesh-work of anastomosing channels or cysts lined by primitive cells with abundant clear to eosinophilic cytoplasm. These features were suggestive of malignant yolk sac tumor (Fig. 3). Resection margins were positive for the tumor. After histopathology results the baby was transferred to pediatric oncology ward. Baseline α-fetoprotein (AFP) was done and found to be elevated to 1000IU/ml and β-human chorionic gonadotropin (β-hCG) was normal (1.06 mIU/L).

After prechemotherapy work-up, she was assigned a diagnosis of sacrococcygeal yolk sac tumor postsurgical stage 3 (pT3b, AII N, M_0). This was consistent with medium risk group 1; therefore, she was planned to receive a total of 4 courses of JEB at 21days interval. Dosage was Bleomycin 4IU IV OD -1/7, Etoposide 32mg IV OD-3/7 and Carboplatin 162mg IV OD -1/7. To counteract side effects, Ondansetron 8mg IV BD -3/7 was given.

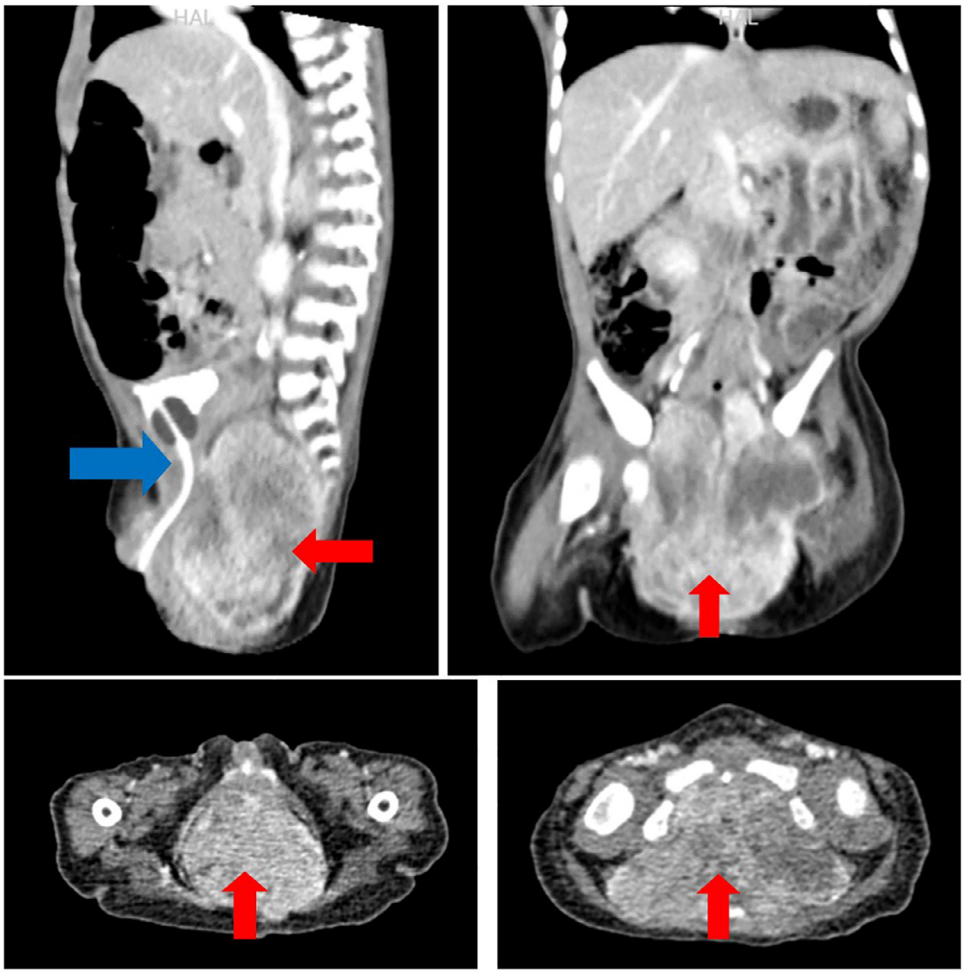

Fig. 1 – CT-scan chest-abdomen-pelvis showed a large heterogeneous enhancing mass (7.6 x 5.3 x 8.4 cm in size) (red) within the pelvis, arising from the sacrococcygeal region, pushing the urinary bladder, rectum and large bowels anteriorly (blue).

End of treatment MRI: There was a regressed sacrococcygeal tumor measuring 2.75 × 2.3 × 2.72 cm in size. It was infiltrating the right sacral nerve root, protruding into the right greater sciatic foramen, abutting adjacent recto-sigmoid reflection and gluteus muscles. No obvious perilesional or intra-abdominal lymphadenopathy seen, however, there was a few inguinal lymph nodes, the largest measuring 1.37 cm by 0.9 cm in size. An uncomplicated inguinal hernia of 1.35 cm size was also noted (Fig. 4).

She was then planned for a second WLE. Intraoperatively, approach was through a sacral inverted V incision, a tumor measuring 2 cm by 1 cm was found in the right side, wide local excision was done, washing with normal saline was done and defect was closed in layers. The tumor was sent for histopathology. Histopathology revealed fibrous tissue with nests of round to oval cells with clear cytoplasm. The cell nuclei were hyperchromatic. This was consistent with residual sacrococcygeal yolk sac tumor.

After second WLE weekly AFP was done, which was progressively rising. Another MRI of the abdomen and pelvis was done 4 weeks later to assess for recurrence or presence of any suprarenal mass. This showed a presacral lesion measuring 3.8 × 4.5 × 4.1 cm. It was infiltrating the right sacral nerve root, protruding into the right greater sciatic foramen and abutting rectosigmoid reflection and gluteus muscles with areas of necrotic changes and granulation tissue on surgical bed, coccygeal cutaneous and postsurgical changes. No obvious suprarenal abnormality, perilesional or intra-abdominal lymphadenopathy was seen (Fig. 5).

She was kept on second line chemotherapy. She received 2 cycles of IV cjemotherapy. During each cycle she received Vinblastin 1.3 mg IV OD for 2 days, Ifosfamide 473 mg IV OD for 5 days, Mesna 150 mg IV OD for 5 days and Cisplatin 7 mg IV OD for 5 days. After treatment AFP was found to be 985 IU/mL. MRI of the pelvis showed sacrococcygeal mass measuring 3.5 × 4.5 × 6.3 cm, with infiltration of the sacral canal up to the level of S2, the right sacral nerve root, extending into the right presacral space and right sciatic foramen. It was also abutting the right 1/3 of the rectum. There features were suggestive of disease progression (Fig. 6). Currently she is on occupational therapy, awaiting a third line chemotherapy after tumor board discussion.

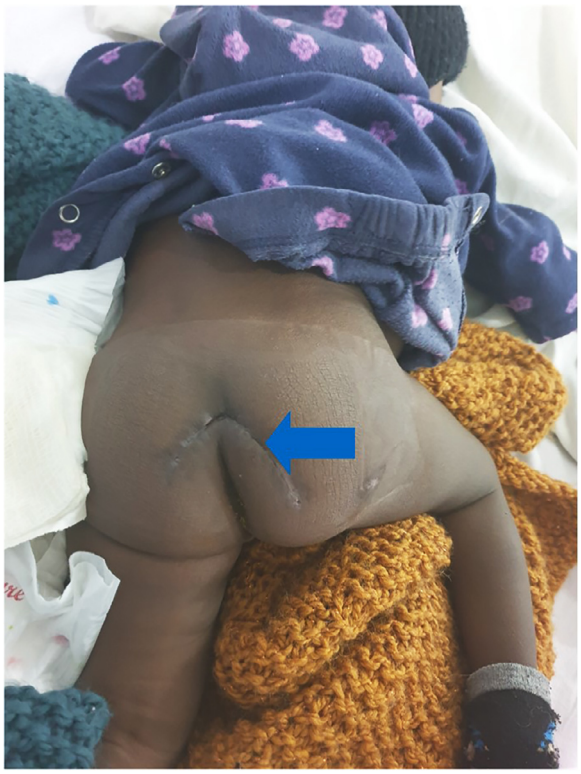

Fig. 2 – Clinical photograph showing postoperative healed surgical incision after first surgery (blue).

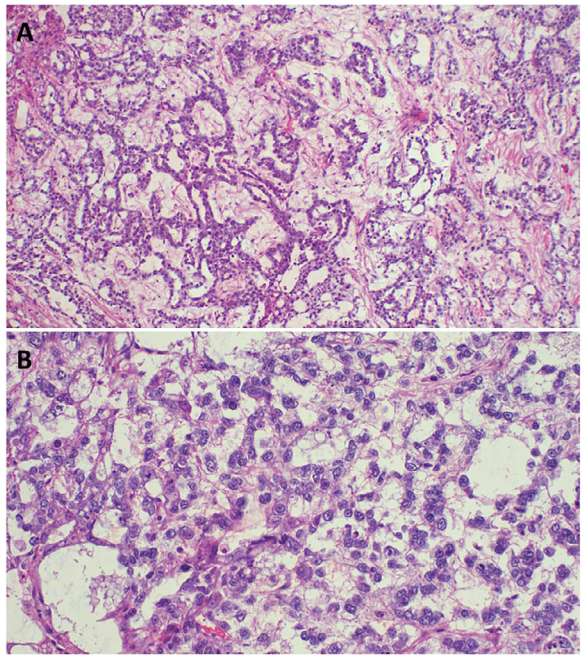

Fig. 3: – (A) Microscopic image of Yolk sac carcinoma demonstrating loose meshwork of anastomosing channels and variably sized cysts (macro or microcysts) lined by primitive tumor cells with varying amounts of clear to eosinophilic cytoplasm; H&E staining 10 x original magnification. (B) Histopathology of Germ cell carcinoma displaying infiltrative tumor with Microscopic image of Yolk sac carcinoma demonstrating loose meshwork of anastomosing channels and variably sized cysts (macro or microcysts) lined by primitive tumor cells with varying amounts of clear to eosinophilic cytoplasm; H&E staining 20 x original magnification.

Discussion

During embryonic development, germ cells arise in the yolk sac in anterior abdominal wall. They migrate along the hind gut of the primitive gut to the gonadal ridge in the posterior abdominal wall where they become incorporated into the gonads. During this migration, some endodermal cells may be left behind close to the midline in the posterior abdominal wall, giving rise to undifferentiated germ cell tumors such as sacrococcygeal yolk sac tumors [6,7].

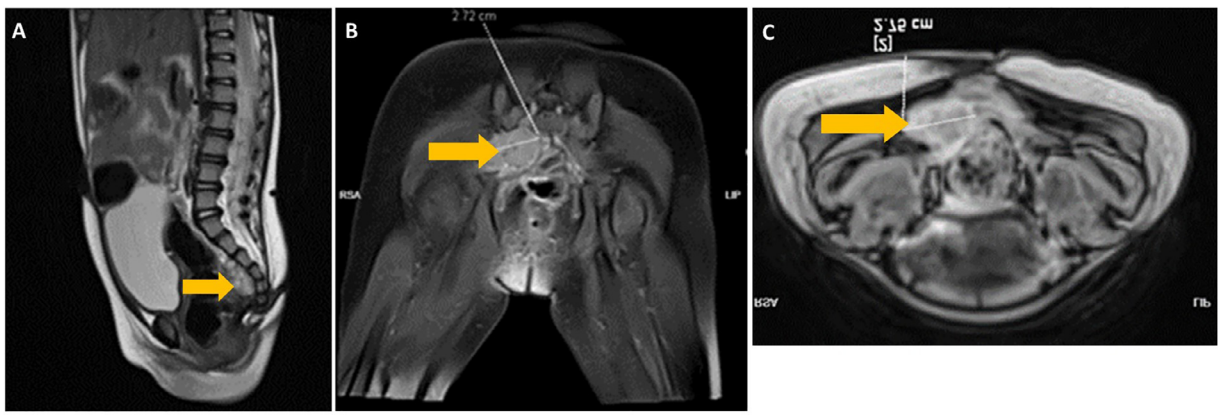

Fig. 4 – MRI pelvis showing sacrococcygeal tumor measuring 2.75 x 2.3 x 2.72 cm in size (yellow). It was infiltrating the right sacral nerve root, protruding into the right greater sciatic foramen, abutting adjacent recto-sigmoid reflection and gluteus muscles.

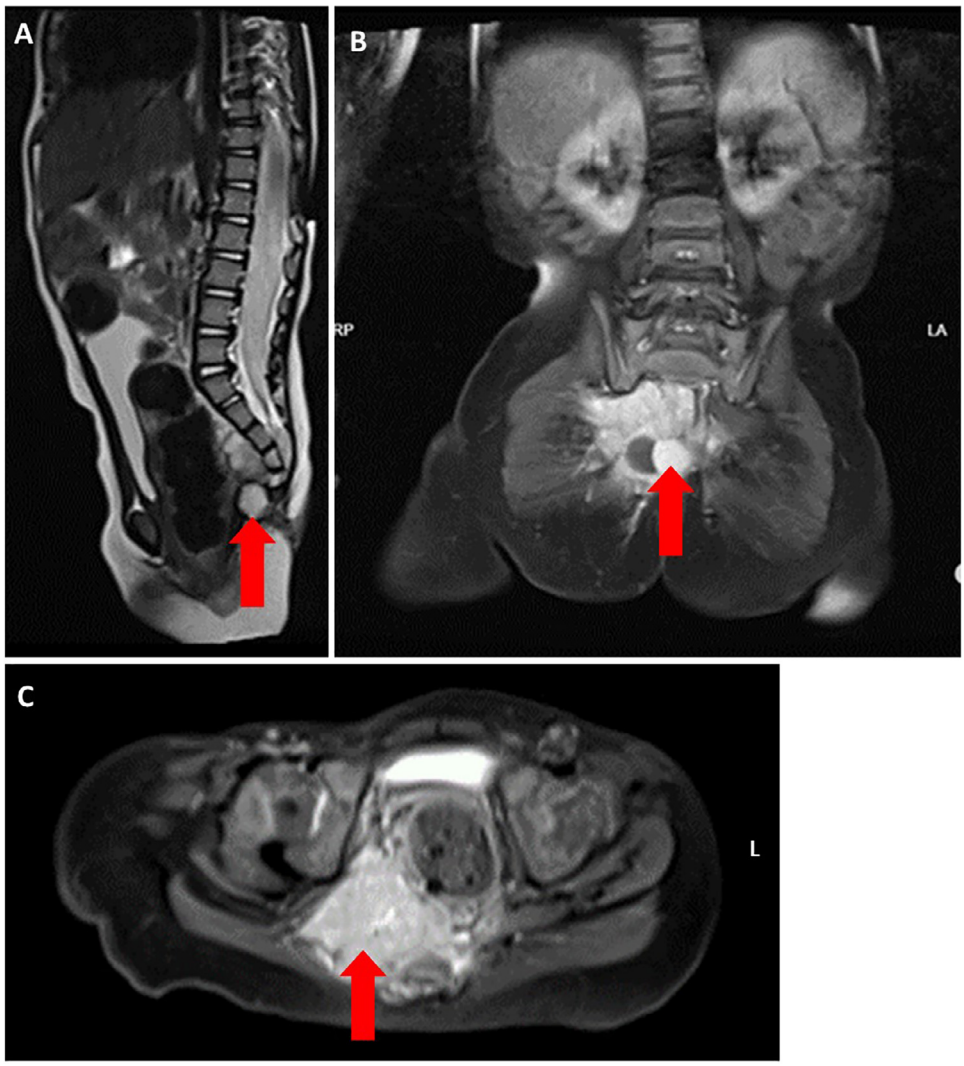

Fig. 5 – MRI abdomen-pelvis showing a presacral lesion measuring 3.8 x 4.5 x 4.1 cm (red). It was infiltrating the right sacral nerve root, protruding into the right greater sciatic foramen and abutting rectosigmoid reflection and gluteus muscles with areas of necrotic changes and granulation tissue on surgical bed, coccygeal cutaneous and postsurgical changes.

GCTs account for about 3% of all pediatric malignancies. Of all GCTs, YSTs constitutes the most common subtype and has the highest risk of malignancy transformation [7,8].

Sacrococcygeal yolk-sac tumors typically present as a palpable mass in the sacrococcygeal area, often noticed at birth or during infancy. Other common clinical features include pain, difficulty with defecation, and urinary symptoms due to compression of nearby structures. Additionally, elevated serum alpha-fetoprotein (AFP) levels are often observed in 95% to 100% of patients. They have a bimodal distribution between children younger than 4 years and adolescents [9,10].

Radiological investigations like CT-scan and MRI play a role in establishing the diagnosis, evaluating extent of local invasion and metastasis and predicting resectability of the tumor. Histological analysis helps to describe a clear diagnosis [11,12]. Some immunohistochemistry (IHC) markers can help pathologists accurately identify yolk sac tumors, particularly in challenging cases where the tumor exhibits mixed histological patterns or when it occurs in extragonadal locations where the differential diagnosis is broader. AFP and Glypican-3 (GPC3) are the most specific and sensitive markers, and when used in conjunction they increase the diagnostic accuracy. Other useful markers include cytokeratin (CK); particularly CK7 and CK19, SALL4, and Placental Alkaline Phosphatase (PLAP). Precise and accurate diagnosis is essential for guiding appropriate treatment [13].

In this case report, the patient was less than 4 years of age, the common age for these tumors. She presented with mild abdominal distension and urinary symptoms for 3 weeks. Also, she had a bulge in the perineum. The clinical presentation was consistent with a congenital mass in the pelvic region impinging on bladder outlet, causing urine retention, leading to abdominal distension. The mass was allowing room for urethral catheterization, a procedure which was relieving the abdominal distension.

An abdominopelvic ultrasound showed a pelvic mass. CT-scan of the chest, abdomen and pelvis was done to evaluate 3D size of the mass, local extension into neighboring

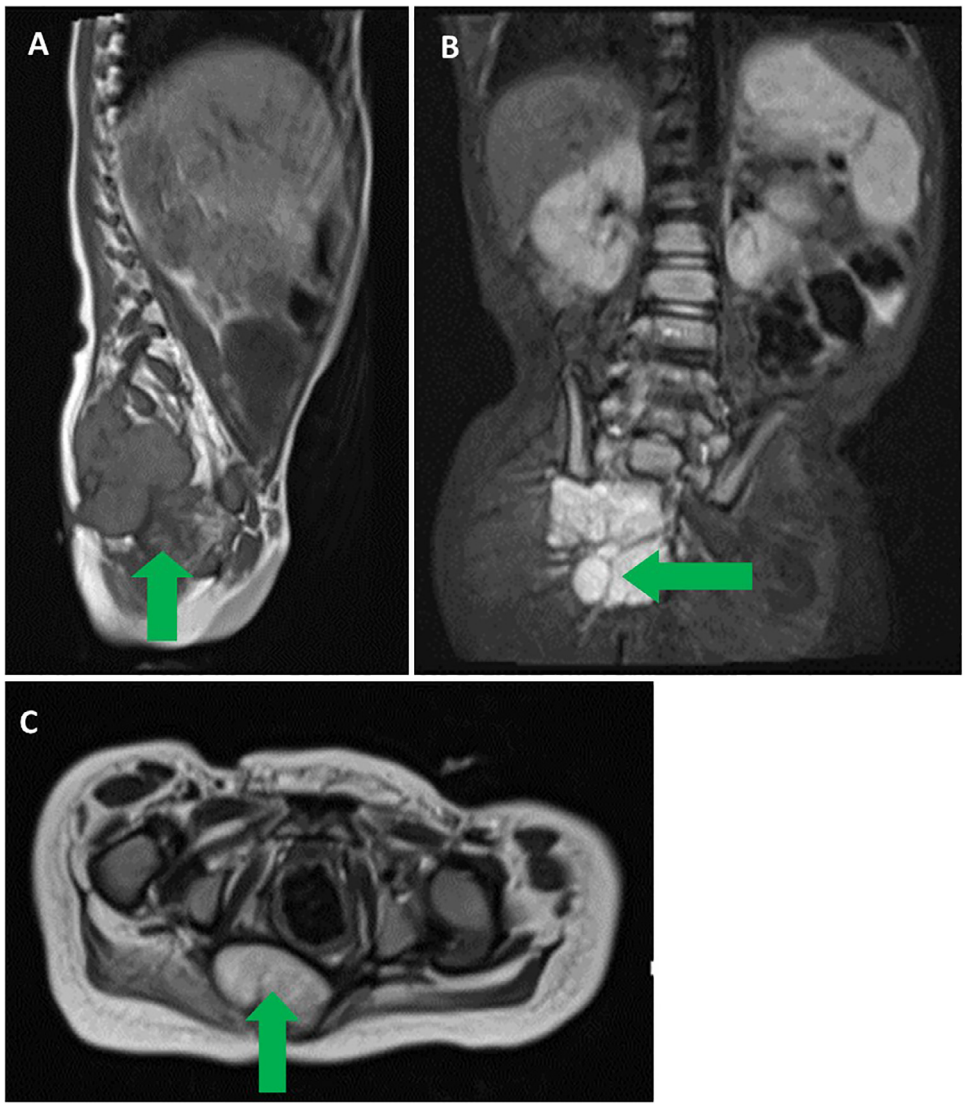

Fig. 6 – Pelvic MRI showing sacrococcygeal mass measuring 3.5 x 4.5 x 6.3 cm, with infiltration of the sacral canal up to the level of S2, suggestive of disease progression (green).

structures and signs of distant metastasis. The mass was arising from sacrococcygeal region, extending to both sacral foramina, with no features of metastasis. Following this imaging, the baby was scheduled for tumor resection, after which the whole specimen was sent for histopathology which concluded yolk-sac tumor. This led to establishment of a definitive diagnosis of malignant sacrococcygeal yolk-sac tumor. Baseline AFP was elevated to 1000IU/ml, while beta-hCG was normal.

Elevated baseline AFB in this patient was not specific because of her age, however, it laid ground for assessment of tumor regression following treatment.

Complete surgical resection is a key factor in favor of good prognosis. The role of chemotherapy after complete surgical resection is controversial, and therefore, watchful waiting is recommended. When complete resection of the tumor is not achieved, consolidation chemotherapy is justified. Radiotherapy has a limited role in treatment of yolk sac tumors. It may be considered in cases of residual disease after chemotherapy when tumor remnants are not surgically resectable, recurrent disease, and in some metastatic sites such as the bone and central nervous system [14–16].

Surgical resection and chemotherapy remain the cornerstone of treatment for MYSTs. Radiotherapy can play a supportive role in managing specific clinical scenarios to control disease progression and improve patient outcomes. The decision to use radiotherapy is typically made on a case-by-case basis, taking into consideration factors such as the location and extent of the tumor, the patient's overall health, and response to the initial treatment [16].

According to Children's Oncology group; extragonadal germ cell tumors that undergo complete tumor resection with coccygectomy, with negative margins, intact tumor capsule, negative peritoneal fluid cytology and lymph nodes $\leq$ 1cm are classified as stage 1. Those with microscopic positive margins, with disruption of tumor capsule, pre or intraoperative biopsy, negative lymph nodes on imaging and negative peritoneal fluid cytology are stage 2.

If there is a gross residual tumor postsurgery, positive lymph nodes, lymph nodes ≥ 2 cm that persist on re-imaging 6 weeks postsurgery are stage 3. Stage 4 tumors present with distant metastasis [9,17,18].

Stage 1 tumors are low risk. They require no chemotherapy. Instead, serum markers (AFP/hCG) should be assessed weekly until they return to normal, then every 4 weeks. Normal AFP may be higher in children below 2 years of age. Stages 2 and 3 in children younger than 11 years are classified as standard risk group 1. They should receive a total of 4 courses of JEB (Carboplatin, Etoposide and Bleomycin) at 21 days interval. Patients with stage 4 tumors are classified as standard risk group 2 and should receive 6 cycles of JEB at 21 days interval [9,17].

If AFP levels have not returned to normal at the end of chemotherapy in both standard risk groups patients, weekly assessment is necessary because it is likely that AFP levels will continue falling thereafter. If imaging shows residual tumor after chemotherapy, second look surgery is warranted provided that there's a possibility of doing nonmutilating resection [9,17].

In the case reported, complete surgical resection was not possible, tumor margins were macroscopically positive and there was no distant metastasis on imaging. The patient was 8-months old at that time. This was consistent with stage 3 disease, medium/standard risk group 1. She was kept of a course of JEB and received 4 cycles as per her risk stratification.

Adolescents and postpuberty patients (≥11 years old) are classified as high-risk patients. In this group, use of Cisplatin based therapies such as BEP (Bleomycin, Etoposide and Cisplatin) is recommended, 4 cycles at 21 days interval. However, use of bleomycin containing therapies in patients with thoracic tumors and renal impairment poses a risk of complications. Bleomycin has the potential of causing lung injury and renal toxicity. In these patients, Carboplatin based chemotherapy is recommended [9,17].

Each cycle of JEB takes 3 days. On day 1 Etoposide 120 mg/m^2 IV is administered over 2-4 hours. On day 2 Etoposide is administered as day 1 and carboplatin is administered based on body weight renal clearance. On day 3 Etoposide is administered as in day 1 and Bleomycin 15,000 IU/m^2 IV over 30 minutes [9,17].

A single cycle of BEP takes 15 days. On day 1, Bleomycin 15,000 IU/m^2, Etoposide 100 mg/m^2 IV and Cisplatin 20 mg/m^2 IV are administered. On days 2 to 5, Etoposide and Cisplatin are administered in doses similar to that of day 1. On days 8 and 15 only Bleomycin is administered as in day 1 [9,17].

At the end of treatment, serum levels of AFP/HCG/LDH should be checked, then monthly for 1 year, then every 2 months for the second year and every 3 months for the third year in secreting tumors. Imaging should be done at the primary site and all sites that were involved at diagnosis [9,17].

In the case presented, end of treatment AFP had fallen to 52I U/ml. However, an MRI showed a residual tumor of about 3 cm by 2 cm by 3 cm. Because of this, she was scheduled for a second tumor resection. This was done at 15 months of age. After that she was kept on surveillance with weekly assessment of AFP. Unfortunately, AFP started rising again. A month after second surgery it had gone back to 1000IU/ml. Another MRI was done which showed a growing mass in presacral region. This was consistent with relapse of the disease. She was then scheduled for second line chemotherapy with Vinblastin, Ifosfamide, Mesna and Cisplatin which is still ongoing.

Prognostic indicators for sacrococcygeal malignant GCTs include stage of the disease, age and baseline AFP levels at diagnosis. AFP levels <1000 ng/mL are in the good prognostic category. Advanced stage of the disease and age older than 11 years at diagnosis are associated with poor prognosis and higher rates of recurrence. In a study done over 25 years, event free survival in patients older than 11 years and with stage 3 or 4 disease, event free survival was <70%. Also delayed diagnosis and incomplete surgical resection at the index surgery result in poor prognosis [9,17,18].

In this case report, an 8-months old female with a stage 3 malignant sacrococcygeal yolk sac tumor and baseline AFP of 1000IU/ml is presented. This was a medium risk group 1 stratification, but stage of the disease at diagnosis and baseline AFP were suggestive of poor prognosis. Despite treatment according to recommended guidelines, the patient had tumor relapse.

Relapse of these tumors is uncommon. In the event of relapse, second line chemotherapy depends on first line agent. Following second line chemotherapy, resection of residual mass is recommended. Radiotherapy is not an integral part of treatment of malignant GCTs. However, it may be considered for individual patients in cases of relapse, recurrence, and metastasis to some sites such as the bones, spinal cord and brain. In addition, use of these platinum-based chemotherapeutic agents poses a risk of ototoxicity in the long run [15,17,18].

Conclusion

Early diagnosis of sacrococcygeal germ cell tumors (SCGCTs) is crucial for improving patient outcomes. Timely identification can significantly impact survival rates, reduce complications, and enhance the quality of life. The management of SCGCTs demands a multidisciplinary approach, involving collaboration among pediatric oncologists, surgeons, radiologists, and pathologists to ensure accurate diagnosis, effective treatment, and long-term monitoring.

Although relapse is rare, it presents a major challenge in managing these tumors, often leading to prolonged hospital stays and increased resource utilization. Relapsed disease complicates treatment and highlights the need for clear, evidence-based guidelines to ensure standardized and effective management of recurrent SCGCTs. Establishing these protocols would not only aid in optimizing patient care but also contribute to the better allocation of healthcare resources.

Author contributions

ESR and JL conceptualized and drafted the manuscript. JL was the lead surgeon. AM reviewed and reported the pathology slides. All authors have read and approved the final script.

Patient consent

Informed consent was obtained from the mother of the infant. Accompanying images have been censored to ensure that the patient cannot be identified. A copy of the consent is available on record.

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